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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/981,685	10/17/2001	Frank L. Graham	ADVEC10IA-C5A	6575

29847 7590 09/10/2003

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EXAMINER	
VOGEL, NANCY T	

ART UNIT	PAPER NUMBER
1636	10

DATE MAILED: 09/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/981,685	GRAHAM ET AL.	
	Examiner	Art Unit	
	Nancy Vogel	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 October 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice to Comply* .

DETAILED ACTION

Claims 1-17 are pending in the application.

This action is in response to the preliminary amendment submitted 10/17/01, Paper No. 7.

Drawings

Applicants are informed that Fig. 6B cannot be incorporated in the specification as requested by applicants in the Response to Notice To File Missing Parts of Application, filed 2/28/02, since the instant application does not include an incorporation by reference of the parent applications.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

Although applicants have stated that the instant application is a continuation of Application No. 09/415,899, the specification of 09/415,899 is not identical to the instant specification. It has been determined that 09/415,899 does not provide support for the claims of the instant application, and therefore the priority date for the instant application has been determined to be the filing date of 10/17/01.

In addition, it is noted that 09/415,866, is not a continuation-in-part of 08/486,549, as stated in applicant's preliminary amendment. Application 09/415,866 claims priority to 09/263,650, as a continuation in part.

Sequence compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. For example, there are sequence in Figure 3-2. These and all sequences in the specification must be listed in the Sequence Listing and must comply with the requirements of 37 CFR 1.821-1.825.

Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. § 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. § 1.136. In no case may an applicant extend the period for response beyond the one month

statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-17 are vague and indefinite in the recitation of "gene". Since the term seems to be used in some of the claims to indicate the coding region without a promoter, while the art accepted meaning normally includes such regulatory elements as the promoter, it is not clear what applicants intend to be encompassed by this term, and the metes and bounds of the claims cannot be determined. It has been assumed for examination purposes that the term "coding sequence" was intended by the term "gene" in the claims.

Claims 2 and 3 are vague and indefinite in their recitation of the terms "operably linked to target sites" (claim 2) and "target sites operably linked to the gene" (claim 3). It is not clear what is intended by this term, since these target sites have no function

except as a target for recombination action of a recombinase, and would function as such independent of orientation or location.

Claims 3-17 are vague and indefinite in their recitation of "alters expression" (claim 3), "resulting in decreased expression" (claims 4, 5, 10, 11, 14, 15), and "resulting in increased expression" (claims 6-9, 12, 13, 16 and 17), since it is not clear to what standard or basal level the expression is being compared. Presumably, the expression level is being compared to that expression level that was present prior to recombination.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 8 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Anton et al. (J. Virology. 69 (8), p. 4600-4606, 1995).

Anton et al. disclose an adenovirus containing a heterologous gene under the control of a recombinase (see page 4603 column 1 second complete paragraph). The reference discloses adenoviruses comprising a gene and site-specific recombinase target sites flanking a DNA spacer located between a promoter sequence and the gene, whereby recombination between said target sites mediated by a site-specific recombinase removes the DNA spacer sequence, resulting in increased expression of the gene (see page 4603, col. 1, second complete paragraph through page 4604, second column, line 47). Said gene (luciferase) is from a non-adenoviral source.

Claims 1-3, 8 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Kanagae et al. (Nucleic Acids Research 23 (19) 3816-3821 (1995)).

Kanagae disclose an adenovirus containing a heterologous gene under the control of a recombinase (see abstract and Fig. 1). The reference discloses adenoviruses comprising a gene and site-specific recombinase target sites flanking a DNA spacer located between a promoter sequence and the gene, whereby recombination between said target sites mediated by a site-specific recombinase removes the DNA spacer sequence, resulting in increased expression of the gene (see abstract, Fig. 1 and page 3819, first column, lines 10-49). Said gene (lacZ) is from a non-adenoviral source.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sauer (US Pat. No. 4,959,317) in view of Berkner (Curr. Top. Microbiol. Immunol., 158:39-66, 1992).

Sauer teaches vectors comprising a gene, the expression of which is under the control of a site-specific recombinase, which is Cre (see column 6, lines 56-column 7, line 24). The reference teaches that recombinase target sites may flank a pre-selected DNA segment, and depending on the orientation of the target sites, may result in inversion or deletion of the DNA segment between the target sites upon expression of the recombinase (see column 3, lines 13-20). The reference discloses a blocking DNA segment flanked by lox sites in the same orientation between a promoter and an engineered gene to render the promoter incapable of expressing the gene. Upon expression of the recombinase gene, the DNA segment is deleted and expression of the engineered gene increases relative to the level present before the deletion (see column 6, lines 56-66). The reference discloses an engineered gene lacking a promoter and flanked by two lox sites in opposite orientation, linked to the transcription start of a regulatory nucleotide sequence such as a promoter. Upon expression of the recombinase cre, the engineered gene is inverted, and expression is increased relative

to the level present before inversion (see column 7, lines 10-24). The reference discloses that any vector may be used, including viruses (column 4, lines 33-35).

The reference does not teach adenoviruses containing a gene under the control of a recombinase, or an adenovirus containing a promoter flanked by recombinase target sites which, upon expression of the recombinase, is inverted or deleted depending on the orientation of the target sites.

Berkner discloses adenoviruses used as vector which contain foreign genes from a non-adenoviral source, under the control of a promoter (see especially pages 50-59). The reference teaches the desirability of using adenovirus vectors for the expression of foreign genes in animal cells (page 40, lines 1-14).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the vectors disclosed by Sauer by the substitution of an adenoviral vector for the vectors exemplified therein, as taught by Berkner, since Sauer teaches that any vector of choice may be used to carry any gene of interest, along with the disclosed recombinase target sites, for control of the expression of the gene of interest, and since as taught by Berkner, it was obvious to one of ordinary skill in the art at the time the invention was made to utilize an adenovirus as a vector for expression of foreign genes in eukaryotic cells. It would have been further obvious to place recombinase target sites on either side of a promoter, since Sauer discloses that any DNA segment may be controlled by a recombinase, through inversion or deletion, when target sites are present (see column 1, lines 1-34)

One would have been motivated to utilize adenoviral vectors for their known and useful properties of ease of transfer of foreign genes into eukaryotic cells, and stability.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy Vogel whose telephone number is (703) 308-4548. The examiner can normally be reached on 7:30 - 4:00, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

REMY YUCEL, PH.D
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TECHNOLOGY CENTER 1600